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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/687,035	10/15/2003	Earl F. Albone	6750-214-999	9476

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EXAMINER	
GODDARD, LAURA B	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 10/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/687,035	ALBONE ET AL.	
	Examiner	Art Unit	
	Laura B. Goddard, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28,44,49-62,77,103-109,116 and 117* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *116 and 117* is/are allowed.

6)☒ Claim(s) *1-28,49-62,77,and 103-109* is/are rejected.

7)☒ Claim(s) *44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The Amendment filed August 10, 2006 in response to the Office Action of May 3, 2006, is acknowledged and has been entered. Previously pending claims 1-6, 12, 44, 49-53, 56, 77, and 117 have been amended. Claims 29-43, 45-48, 63-76, 78-102, 110-115, and 118-119 are canceled. Claims 1-28, 44, 49-62, 77, 103-109, 116, and 117 are currently being examined.

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Claim Objections

3. Claim 44 appears to be free of the art but is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

NEW REJECTIONS

(necessitated by amendment)

Claim Rejections - 35 USC § 112

4. Claims 1-28, 49-62, 77, and 103-109 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 1 and 77 recite the phrase "**repeat region** within SEQ ID NO:1" or "**repeat region** present within SEQ ID

NO:1". It is unclear what sequence represents the repeat region and where the antibody or fragment is binding to. Although the specification delineates "repeat regions" in SEQ ID NO:1, Figure 1 and 2, these regions do not appear to be repeats and represent different sequences. O'Brien et al (Tumour Biol, 2001, 22:345-66) teach that the extracellular domain of the CA 125 antigen is characterized by a large number of repeats (probably 60+) (abstract). Further, although the claims are read in light of the specification, limitations recited in the specification are not read into the claims.

5. Claims 1-28, 49-62, 77, and 103-109, are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection.

The claims are drawn to an isolated antibody or an antigen-binding antibody fragment, that preferentially binds cell-associated CA 125/O772 polypeptide relative to shed CA 125/O772P polypeptide, wherein the isolated antibody, or the antigen binding antibody fragment, binds a **repeat region within SEQ ID NO:1** (claims 1-28, 49-62, 103-109), and a fusion polypeptide comprising an antibody, or an antigen-binding antibody fragment, which preferentially binds cell-associated CA 125/O772P relative to shed CA 125/O772P, wherein the isolated antibody or the antigen binding antibody

fragment bind **a repeat region present within SEQ ID NO:1,** operably linked to a heterologous agent (claim 77).

The specification discloses that Figure 1 depicts the amino acid sequence of CA 125/O772P 3-repeat (SEQ ID NO:1) and comprises a repeat region within amino acids 14-452 (Figure 1; p. 22, [0084]). The specification discloses three repeat regions within the 14-452 repeat region as delineated in Figure 1 and 2. The specification does not disclose any other repeat regions within as broadly encompassed in the claims.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of "repeat region within SEQ ID NO:1". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like

a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted

the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here.

Thus, the instant specification may provide an adequate written description of a repeat region within SEQ ID NO:1, per Lilly by structurally describing representative repeat regions within SEQ ID NO:1 or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe a repeat region within SEQ ID NO:1 useful in the claimed invention in a manner that satisfies either the Lilly or Enzo standards. Although the specification discloses three specific repeat regions delineated in SEQ ID NO:1, this does not provide a description of the broadly claimed repeat regions within SEQ ID NO:1 that would satisfy the standard set out in Enzo

because the specification provides no functional characteristics coupled to structural features.

Further, the specification also fails to describe repeat regions within SEQ ID NO:1 by the test set out in Lilly because the specification describes only three specific repeat regions in SEQ ID NO:1. Therefore it necessarily fails to describe a representative number of such species.

Thus, the specification does not provide an adequate written description of a repeat region within SEQ ID NO:1 that is required to practice the claimed invention.

MAITAINED REJECTION

Claim Rejections - 35 USC § 112

6. **Claims 54 and 55 remain rejected under 35 U.S.C. 112, first paragraph**, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a WRITTEN DESCRIPTION rejection (see previous Office Action, section 9, pages 6-13).

The claims are drawn to the antibody or antigen-binding antibody fragment of Claim 1, wherein the antibody or antigen-binding antibody fragment is **modified by amino acid substitution, deletion, or addition, or a combination thereof** and has the same or increased affinity for cell-associated CA 125/O772P relative to that of a corresponding unmodified antibody or antigen-binding antibody fragment (claim 54),

and wherein the antibody or antigen-binding antibody fragment is **modified by amino acid substitution, deletion, or addition, or a combination thereof** and exhibits the same or an increased serum half-life compared to that of a corresponding unmodified antibody or antigen-binding antibody fragment (claim 55).

The specification discloses antibodies in Tables 7 and 8, page 83 that are specific for CA 125/O772P polypeptide (SEQ ID NO:1) (p. 82). The specification discloses antibodies in Table 11 and 12 that preferentially bind cell-associated CA 125/O772P polypeptide (p. 87-88). A flow cytometry competition assay identified antibodies that preferentially bind to cell-associated CA 125/O772P polypeptide relative to shed CA 125/O772P polypeptide (p. 88-89, Tables 13 and 10). A BIAcore affinity assay identified antibodies that bind with high affinity to CA 125/O772P polypeptide (p. 90, Table 14). An ADCC assay identified antibody117.1 as capable of mediating lysis of ovarian cancer cells in a dose-dependent manner (p. 91-92; Fig. 4). The specification discloses the sequences of antibodies that preferentially bind cell-associated CA 125/O772P polypeptide relative to shed CA 125/O772P polypeptide (p. 6-8; Figs. 5A–10D; p. 92-94) and the hybridomas producing said antibodies (p. 9). The specification discloses SEQ ID NO:1 and 2 as sequences of a CA 125/O772P polypeptide.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any

combination thereof. In this case, the only factor present in the claim is a recitation of "modified by amino acid substitution, deletion, or addition, or a combination thereof", "has the same or increased affinity for cell-associated CA 125/O772P relative to that of a corresponding unmodified antibody", or "exhibits the same or an increased serum half-life compared to that of a corresponding unmodified antibody". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus.

Although drawn to DNA arts, the findings in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and Enzo Biochem, Inc. V. Gen-Probe Inc. are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in University of California v. Eli Lilly and Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that " [a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name', of the claimed subject matter sufficient to distinguish it from other materials. " Id. At 1567, 43 USPQ2d at 1405. The court also stated that:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicated,

does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. At 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." Id.

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See Enzo Biochem, Inc. V. Gen-Probe Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The Enzo court adopted the standard that "the written description requirement can be met by show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics ....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. At 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in Lilly and Enzo were DNA constructs per se, the holdings of those cases are also applicable to claims such as those at issue here. Thus,

the instant specification may provide an adequate written description the claimed antibody, hybridoma, and pharmaceutical composition, per Lilly by structurally describing representative shed and cell-associated CA 125/O772P polypeptides or by describing specific antibodies with the claimed characteristics as stated above or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics."

In this case, the specification does not directly describe antibodies modified by amino acid substitution, deletion, or addition, or a combination thereof with the claimed functions stated above useful in the claimed invention in a manner that satisfies either the Lilly or Enzo standards. **There are no structural features associated with the various claimed functions and characteristics of the antibodies.** The specification describes deposited antibodies and sequences of antibodies that preferentially bind cell-associated CA 125/O772P polypeptide relative to shed CA 125/O772P polypeptide, these antibodies provide structural features associated with the claimed function of preferentially binding cell-associated CA 125/O772P polypeptide relative to shed CA 125/O772P polypeptide. Although the specification discloses SEQ ID NO:1 and 2 and deposited antibodies, this does not provide a description of the broadly claimed antibodies or fragments that are modified by amino acid substitution, deletion, or

addition that would satisfy the standard set out in Enzo because the specification provides no functional characteristics coupled to **structural features**.

Further, the specification also fails to describe antibodies that are modified by amino acid substitution, deletion, or addition, by the test set out in Lilly because the specification describes only SEQ ID NO:1 and 2 and deposited antibodies that preferentially bind cell-associated CA 125/O772P polypeptide relative to shed CA 125/O772P polypeptide. Therefore it necessarily fails to describe a representative number of such species of antibody modified by amino acid substitution, deletion, or addition that have the same or increased affinity for cell-associated CA 125/O772P relative to that of a corresponding unmodified antibody or that exhibit the same or increased serum half-life compared to a corresponding unmodified antibody.

Thus, the specification does not provide an adequate written description of an antibody modified by amino acid substitution, deletion, or addition that is required to practice the claimed invention.

Response to Arguments

7. Applicants argue that the instant specification conveyed with reasonable clarity to those skilled in the art, as of the earliest claimed priority date, that Applicants were on possession of the subject matter of amended claims 1-24, 49-62 and 103-106. Applicants argue that the amended claim 1 recites an antibody that, *inter alia,* binds a repeat region presented within SEQ ID NO:1, and the specification teaches that this repeat region is preferentially present in cell-associated CA 125/O772P polypeptide,

hence, the specification describes the genus of antibodies that preferentially bind cell-associated CA 125/O772P polypeptide recited in claim 1 and in the claims that depend from claim 1 (p. 14).

The argument has been considered but is not found persuasive because Applicants have not provided the structural characteristics of the repeat region in the claims that is associated with the function of preferentially binding cell-associated CA 125/O772P polypeptide as opposed to shed. As stated above: "To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claim is a recitation of "repeat region within SEQ ID NO:1". Accordingly, in the absence of sufficient recitation of distinguishing identifying characteristics, the specification does not provide adequate written description of the claimed genus." "Thus, the instant specification may provide an adequate written description of a repeat region within SEQ ID NO:1, per Lilly by structurally describing representative repeat regions within SEQ ID NO:1 or by describing "structural features common to the members of the genus, which features constitute a substantial portion of the genus." Alternatively, per Enzo, the specification can show that the claimed invention is complete "by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a known or disclosed

correlation between function and structure, or some combination of such characteristics."

Claims 54 and 55 remain rejected under 35 USC 112 first paragraph, written description because the claims do not provide structural characteristics associated with the functions in the claims as explained in section 6 above. Applicants do not specifically address the lack of structure of the antibody "modified by amino acid substitution, deletion, or addition, or a combination thereof" associated with the claimed functions.

8. All other rejections and objections recited in the Office Action mailed May 3, 2006 are hereby withdrawn. Applicants submitted a "Statement Regarding Permanence and Availability of Deposited Hybridomas" to overcome the 112 1st paragraph written description/deposit rejection in section 8, p. 5-6, of the previous Office Action. Applicants amended claim 117 to recite "isolated antibody" to overcome the 101 rejection in section 5, p. 3, of the previous Office Action. Applicants canceled claims 25, 32, 38, 63-76, 110-112, and 118 to overcome the 112 1st enablement rejections in sections 10 and 11, p. 13-22, of the previous Office Action. Applicants canceled claim 119 to overcome the 102(b) rejections in sections 12 and 13, p. 22-24, of the previous Office Action.

9. **Conclusion:** Claims 116 and 117 appear to be allowable. Claim 44 is objected to. Claims 1-28, 49-62, 77, and 103-109 are rejected under 35 U.S.C. 112, first and second paragraphs.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. ' 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Laura B. Goddard, Ph.D. whose telephone number is (571) 272-8788. The examiner can normally be reached on 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Laura B Goddard, Ph.D.
Examiner
Art Unit 1642

JEFFREY SIEW
SUPERVISORY PATENT EXAMINER